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US government orders new look at dioxin

The Environmental Protection Agency is evaluating data from the past decade that suggest dioxin's toxicity may be overestimated. A risk assessment model based on biological mechanism is being drawn up.

DIOXIN is widely thought of in the United States as the most toxic chemical known to man. As a component of the infamous Agent Orange that the US used to defoliate the jungles of Vietnam, after the war dioxin was blamed for cancer in servicemen who saw duty there. Although compensation was finally offered, neither solid epidemiological nor biological proof of cause and effect has been conclusively demonstrated.

When a chemical plant exploded at Seveso, Italy in 1976, spewing dioxin-contaminated agents into the air, it was feared (and assumed) that the exposed citizens of the town would experience increased cases of cancer and/or birth defects. In fact, severe chlorachne was reported but, fortunately, more life-threatening diseases were not.

When, in 1982, the soil in the small town of Times Beach, Missouri was found to be contaminated by dioxin at levels around 1 part per million, US government officials closed the town down permanently and evacuated its 2,000 residents to safer ground across the river. Nearly a decade later, clean-up work is still going on. Someday, when the soil is incinerated and the buildings are all torn down, Times Beach may be turned into a park.

Over the years, hundreds of millions of dollars have been spent getting rid of dioxin, which has earned its reputation as a killer because it is highly carcinogenic in guinea pigs and and causes birth defects in mice exposed to small concentrations of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin or TCDD.

Now, into this politically charged arena comes William K. Reilly, the head of the US Environmental Protection Agency, saying that dioxin may not be so exceptionally toxic after all. During the past several years, data in humans has accumulated that question the validity of extrapolating TCDD data from guinea pigs to man. Reilly has called for a total re-evaluation of dioxin in all of its many chemical forms (there are 75 or so).

It takes a brave man to put scientific evidence ahead of deeply ingrained public opinion. The last time a federal official suggested that dioxin standards could be relaxed was in 1989 when Vernon Houck of the Centers for Disease Control in Atlanta advised the state of Georgia about water standards. Shortly thereafter, he was subjected to a congressional inquiry into his possible bias toward the paper industry which puts dioxin-contaminated wastes into streams after bleaching pulp. Houck stood his ground, testifying that "new information indicates that we should be less concerned than we once were."

In March of this year, Reilly and other top EPA officials received a briefing on dioxin that Reilly credits for his change of mind. First, his advisers reported an unusual consensus from a recent dioxin conference at the Banbury Center at Cold Spring Harbor, New York. Researchers agreed that the toxicity of TCDD depends upon its binding with the aromatic hydrocarbon receptor, or Ah. Most to the point, they agreed that receptor binding mediates TCDD toxicity in virtually every test system studied, and that receptor binding needs to occur in thousands of cells, though the dividing line between safe and toxic concentrations is not known.

Nevertheless, this observation leads directly to Reilly's conclusion that "work should begin on a new biologically-based model for assessing the toxicity of dioxin." Until now, the Environmental Protection Agency has relied on the standard linear multistage model that predicts no threshold of safety. Based on this model, US standards for exposure to 'background' levels of dioxin that is in the environment are stringent: .006 picograms per kg body weight per day for intake from food or water, for instance. Interestingly, Canadian and European scientists generally have not accepted the US position that dioxin is the most toxic chemical around. Conservative estimates put a safe dioxin intake at 1 picogram per kg per day, while more liberal standards go as high as 10 picograms per kg. Although no changes in US regulations have been put forward, it is likely that the US will move in the direction of its neighbours abroad.

A second bit of data that figured in Reilly's request for a new look at dioxin comes from a large epidemiological study reported in the 24 January issue of *The New England Journal of Medicine*. Researchers at the US National Institute for Occupational Safety and Health in Cincinnati, Ohio, conducted a retrospective mortality study of 5,172 workers at 12 chemical plants that produce agents in which TCDD is a contaminant. Their conclusions: "Mortality from several cancers previously associated with TCDD (stomach, liver, and nasal cancers, Hodgkin's disease and non-Hodgkin's lymphoma) was not significantly elevated in this cohort. Mortality from soft-tissue sarcoma was increased but not significantly."

Government scientists, working with colleagues in universities, have been asked not only to develop a biologically based or receptor model, but also to construct a plan for evaluating the new epidemiological data so that any new standard-setting regulations encompass the new data as a whole. March of 1992 is the target date for completion of the work.

Environmental Protection Agency scientists seem to be fully aware that they are entering dangerous territory. Even though data may exonerate dioxin somewhat, it remains a toxic contaminant of the environment that has no compensating benefit. Furthermore, a reassessment of dioxin has obvious implications for related polychlorinated biphenyls. Ultimately, it could lead to a biologically based model for any agent or group of agents for which toxicity is understood at a mechanistic level.

That the government must proceed carefully, and openly, is vital. Reilly has promised independent scientific review, which is certain to be subject to harsh scrutiny by groups committed to the view that the only acceptable risk is no risk at all. Over the years, this has become the unstated goal of many groups in the United States, but with science's ability to measure chemicals at ever smaller concentrations, it becomes crucial to rank toxic compounds in some sensible order of hazard. As Reilly has noted, "There simply are more anxieties than we can possibly create laws to alleviate, and far more risks than resources to eliminate them."

There is no doubt that a decision to declare dioxin less hazardous will be painful, particularly to the people at Times Beach and elsewhere whose lives have been so totally disrupted. At the time steps were taken to evacuate the town, the decision was entirely in keeping with scientific data available. Human data were scarce. It was thought prudent to rely on animal data and they made a strong case for judging dioxin to be unusually toxic. Although researchers may be comfortable with the idea that new judgements should correctly follow new data, it remains a difficult concept for the public.

Nevertheless, it is time to set priorities, even if it is politically treacherous.

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